
Immunosuppressive Treatment Can Alter Visual Performance in the RCS Rat.

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Public Summary:

Purpose: Immunosuppression is frequently employed to enhance survival of xenografted human cells as part of translational proof-of-concept studies. However, the potential effects of this treatment are easily overlooked. **Methods:** As part of baseline testing in the dark-eyed variant of the dystrophic Royal College of Surgeons (RCS) rat, we documented the time course of retinal degenerative changes versus Long Evans controls using bright field retinal imaging, fluorescein angiography, and histology and examined the impact of immunosuppression on visual function. Rats received either no treatment or systemic immunosuppression with oral cyclosporine A and injectable dexamethasone and subsequently underwent functional evaluation by optomotor response testing and electroretinography (ERG) at multiple intervals from P45 to P180. **Results:** Immunosuppressed RCS animals demonstrated poorer performance on functional tests than age-matched untreated rats during the earlier stages of degeneration, including significantly lower spatial acuities on optomotor threshold testing and significantly lower b-wave amplitudes on scotopic and photopic ERGs. Retinal imaging documented the progression of degenerative changes in the RCS fundus and histologic evaluation of the RCS retina confirmed progressive thinning of the outer nuclear layer. **Conclusions:** A standard regimen of cyclosporine A plus dexamethasone, administered to RCS rats, results in demonstrable systemic side effects and depressed scores on behavioral and electrophysiological testing at time points before P90. The source of the functional impairment was not identified. This finding has implications for the interpretation of data generated using this commonly used translational model.

Scientific Abstract:

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